

CLAIMS

1. (Withdrawn) A method of producing a cell-permeable osteoinductive polypeptide comprising introducing into a suitable host cell an expression construct comprising: a) a polynucleotide encoding a cell-permeable polypeptide; b) a polynucleotide encoding an osteoinductive polypeptide operably linked to the cell-permeable polypeptide and positioned so that the osteoinductive polypeptide is expressed as part of a fusion protein with the cell-permeable polypeptide; c) a promoter positioned to direct transcription of the polynucleotides.
2. (Withdrawn) The method of claim 1 wherein the expression construct further comprises a purification tag.
3. (Withdrawn) The method of claim 1 wherein the cell-permeable polypeptide is chosen from the group consisting of HIV-TAT, VP-22, a growth factor signal peptide sequence, Pep-1, and a Drosophila Antp peptide.
4. (Withdrawn) The method of claim 1 wherein the cell-permeable polypeptide is an HIV-TAT protein transduction domain.
5. (Withdrawn) The method of claim 1 wherein the osteoinductive polypeptide is chosen from the group consisting of LMP-1, LMP-3, SEQ ID NO 1, SEQ ID NO 2, SEQ ID NO 3, SEQ ID NO 4, SEQ ID NO 5, SEQ ID NO 6, SEQ ID NO 7, SEQ ID NO 8, BMP-2, BMP-4, BMP-6, BMP-7, TGF-beta 1 and Smad.
6. (Withdrawn) The method of claim 1 wherein the osteoinductive polypeptide is chosen from the group consisting of LMP-1, LMP-3, SEQ ID NO 1, SEQ ID NO 2, SEQ ID NO 3, SEQ ID NO 4, SEQ ID NO 5, SEQ ID NO 6, SEQ ID NO 7, and SEQ ID NO 8.
7. (Currently Amended) A method of inducing bone formation in a mammal comprising administering an effective amount of a fusion polypeptide comprising a protein transduction domain and at least one isolated osteoinductive polypeptide region of an LMP-1 protein or an LMP-3 protein.

8. (Original) The method of claim 7 wherein the protein transduction domain is chosen from the group consisting of HIV-TAT, VP-22, a growth factor signal peptide sequence, Pep-i, and a Drosophila Antp peptide.
9. (Original) The method of claim 7 wherein the protein transduction domain is an HIV-TAT protein transduction domain.
10. (Currently Amended) The method of claim 7 wherein the osteoinductive polypeptide is chosen from the group consisting of ~~LMP-1, LMP-3~~, SEQ ID NO 1, SEQ ID NO 2, SEQ ID NO 3, SEQ ID NO 4, SEQ ID NO 5, SEQ ID NO 6, SEQ ID NO 7, SEQ ID NO 8 and combinations thereof.
11. (Currently Amended) The method of claim 7 wherein the osteoinductive polypeptide comprises ~~LMP-1, LMP-3~~, SEQ ID NO 7, or SEQ ID NO 8.
12. (Original) The method of claim 7 wherein the fusion polypeptide is administered as an implant.
13. (Original) The method of claim 7 wherein the fusion polypeptide is administered by hydrogel.
14. (Original) The method of claim 7 wherein the fusion polypeptide is administered to at least one multipotent progenitor cell.
15. (Original) The method of claim 14 wherein the at least one multipotent progenitor cell is implanted into the mammal.
16. (Withdrawn) A polynucleotide encoding a fusion protein comprising a protein transduction domain and at least one osteoinductive polypeptide.

17. (Withdrawn) The polynucleotide of claim 16 wherein the protein transduction domain is chosen from the group consisting of HIV-TAT, VP-22, a growth factor signal peptide sequence, Pep-1, and a Drosophila Antp peptide.

18. (Withdrawn) The polynucleotide of claim 16 wherein the protein transduction domain is an HIV-TAT protein transduction domain.

19. (Withdrawn) The polynucleotide of claim 16 wherein the osteoinductive polypeptide is chosen from the group consisting of LMP-1, LMP-3, SEQ ID NO 1, SEQ ID NO 2, SEQ ID NO 3, SEQ ID NO 4, SEQ ID NO 5, SEQ ID NO 6, SEQ ID NO 7, SEQ ID NO 8, BMP-2, BMP-4, BMP-6, BMP-7, TGF-beta 1 and Smad.

20. (Withdrawn) The polynucleotide of claim 16 wherein the osteoinductive polypeptide is chosen from the group consisting of LMP-1, LMP-3, SEQ ID NO 1, SEQ ID NO 2, SEQ ID NO 3, SEQ ID NO 4, SEQ ID NO 5, SEQ ID NO 6, SEQ ID NO 7, and SEQ ID NO 8.

21. (Currently Amended) A method of inducing proteoglycan synthesis in a mammal comprising administering an effective amount of a fusion polypeptide comprising a protein transduction domain and at least one isolated osteoinductive polypeptide region of an LMP-1 protein or an LMP-3 protein, wherein the proteoglycan concentration prior to said administering step is less than said concentration post said administering step.

22. (Original) The method of claim 21 wherein the protein transduction domain is chosen from the group consisting of HIV-TAT, VP-22, a growth factor signal peptide sequence, Pep-1, and a Drosophila Antp peptide.

23. (Original) The method of claim 21 wherein the protein transduction domain is an HIV-TAT protein transduction domain.

24. (Currently Amended) The method of claim 21 wherein the osteoinductive polypeptide is chosen from the group consisting of ~~LMP-1, LMP-3~~, SEQ ID NO 1, SEQ ID NO 2, SEQ ID NO

3, SEQ ID NO 4, SEQ ID NO 5, SEQ ID NO 6, SEQ ID NO 7, SEQ ID NO 8 and combinations thereof.

25. (Currently Amended) The method of claim 21 wherein the osteoinductive polypeptide comprises ~~LMP-1, LMP-3~~, SEQ ID NO: 7 or SEQ ID NO: 8.

26. (Original) The method of claim 21 wherein the fusion polypeptide is administered as an implant.

27. (Original) The method of claim 21 wherein the fusion polypeptide is administered by hydrogel.

28. (Original) The method of claim 21 wherein the fusion polypeptide is administered to at least one multipotent progenitor cell.

29. (Original) The method of claim 21 wherein the at least one multipotent progenitor cell is implanted into the mammal.

30. (Original) The method of claim 21 wherein the proteoglycan is aggrecan.

31. (Withdrawn) An isolated fusion polypeptide comprising a membrane-translocating peptide operably linked to an osteoinductive polypeptide.

32. (Withdrawn) The method of claim 31 wherein the membrane-translocating peptide is chosen from the group consisting of HIV-TAT, VP-22, a growth factor signal peptide sequence, Pep-1, and a Drosophila Antp peptide.

33. (Withdrawn) The method of claim 31 wherein the membrane-translocating peptide is an HIV-TAT protein transduction domain.

34. (Withdrawn) The method of claim 31 wherein the osteoinductive polypeptide is chosen from the group consisting of LMP-1, LMP-3, SEQ ID NO 1, SEQ ID NO 2, SEQ ID NO 3, SEQ ID NO 4, SEQ ID NO 5, SEQ ID NO 6, SEQ ID NO 7, SEQ ID NO 8.

35. (Withdrawn) The method of claim 31 wherein the osteoinductive polypeptide comprises LMP-1, LMP-3, SEQ ID NO 7, or SEQ ID NO 8.

36. (Currently Amended) A method of inducing osteoblast differentiation in a progenitor cell, the method comprising administering to the progenitor cell an effective amount of a fusion polypeptide comprising a protein transduction domain and at least one isolated osteoinductive polypeptide region of an LMP-1 protein or an LMP-3 protein, wherein the differentiated osteoblast concentration prior to said administering step is less than said concentration post said administering step.

37. (Original) The method of claim 36 wherein the protein transduction domain is chosen from the group consisting of HIV-TAT, VP-22, a growth factor signal peptide sequence, Pep-1, and a Drosophila Antp peptide.

38. (Original) The method of claim 36 wherein the protein transduction domain is an HIV-TAT protein transduction domain.

39. (Currently Amended) The method of claim 36 wherein the osteoinductive polypeptide is chosen from the group consisting of ~~LMP-1, LMP-3~~, SEQ ID NO 1, SEQ ID NO 2, SEQ ID NO 3, SEQ ID NO 4, SEQ ID NO 5, SEQ ID NO 6, SEQ ID NO 7, SEQ ID NO 8 and combinations thereof.

40. (Currently Amended) The method of claim 36 wherein the osteoinductive polypeptide comprises ~~LMP-1, LMP-3~~, SEQ ID NO 7, or SEQ ID NO 8.

41. (Withdrawn) An osteoinductive polypeptide chosen from among the group consisting of SEQ ID NO 1, SEQ ID NO 2, SEQ ID NO 3, SEQ ID NO 4, SEQ ID NO 5, SEQ ID NO 6, SEQ ID NO 7, and SEQ ID NO 8, or combinations thereof.

42. (Withdrawn) An osteoinductive polypeptide which hybridizes under standard conditions to a nucleic acid molecule complementary to the sequence: tctcatccg ggtcttgcac gaactcggcg.

43. (Withdrawn) An osteoinductive polypeptide which hybridizes under highly stringent conditions to a nucleic acid molecule complementary to the sequence: gccccgcgcc gctgacagcg ccccgcaa.